

## Effect of *Yinian Jiangya Yin* on Primary Hypertension in Early Stage — A Clinical Observations on 40 Patients

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**Objective:** To observe the effect of *Yinian Jiangya Yin* (Decoction for lowering blood pressure to prolong life) on patients with early hypertension and its mechanism on the function of vascular endotheliocytes. **Methods:** The 79 patients with early primary hypertension belonging to the TCM syndrome of stagnation of phlegm and blood stasis in meridians and hyperactivity of the liver-*yang* were randomly divided into a treatment group of 40 patients treated with *Yinian Jiangya Yin* and a control group of 39 patients treated with *Tianma Gouteng Yin* (Decoction of Gastrodia and Uncaria). The changes in score of TCM syndrome and in blood pressure before and after treatment were observed in the two groups. The contents of nitrogen monoxide (NO) and endothelin (ET) in serum after treatment were determined. **Results:** There was a statistical difference ( $P < 0.05$ ) in score of TCM syndrome, effect of lowering blood pressure, and the contents of ET and NO in serum after treatment between the two groups. **Conclusion:** The effect of *Yinian Jiangya Yin* on improving TCM syndrome of patients with primary hypertension in early stage and on lowering blood pressure may be related to its regulating the imbalanced condition between ET and NO for restoring the function of endothelium-dependent vasodilation.

**Key words:** *Yinian Jiangya Yin*; primary hypertension; endothelial function; stagnation of phlegm and blood stasis in meridians; hyperactivity of the liver-*yang*

Dysfunction of endothelium-dependent vasodilation, a manifestation of early hypertension, causes the remodeling of blood vessels and damage to target organs. In the late stage, the rise of blood pressure and damage to target organs aggravate lesion of vascular endothelium.<sup>1</sup> Imbalance between endothelium-dependent systolic factor and diastolic factor decreases the release of nitrogen monoxide (NO) and increases the secretion of endothelin (ET). In the research, the authors used *Yinian Jiangya Yin* to treat primary hypertension in early stage and observed its influence on NO and ET in serum and its possible mechanism on primary hypertension in early stage.

### CLINICAL MATERIALS

#### General Data

The 79 outpatients aged 40–60 at the Hospital affiliated to Macao University of Science and

Technology and the First Hospital affiliated to Guangzhou University of Chinese Medicine were randomly divided into a treatment group, 40 patients, 17 males and 23 females, aged  $51.70 \pm 4.53$  on average, and a control group, 39 patients, 18 males and 21 females, aged  $51.67 \pm 4.36$  on average. There was no statistical difference ( $P > 0.05$ ) in sex and age between the two groups, hence compatible.

#### Diagnosis

In reference to the standard for diagnosing grade I hypertension (mild) stipulated by World Health

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Organization International Society of Hypertension in 1999,<sup>2</sup> diagnostic standard in western medicine defines systolic blood pressure (SBP) as  $\geq 140$  mmHg and  $\leq 159$  mmHg, or diastolic blood pressure (DBP) as  $\geq 90$  mmHg and  $\leq 99$  mmHg, patients with SBP  $\geq 140$  mmHg and  $\leq 159$  mmHg, or DBP  $\geq 90$  mmHg and  $\leq 99$  mmHg conform to the standard.

In reference to *the Principle for Guiding Clinical Research on New Chinese Drugs*,<sup>3</sup> standard for diagnosing TCM syndrome defines the main symptoms of stagnation of phlegm and blood stasis in meridians and hyperactivity of the liver-*yang* as dizziness, headache, heavy sensation in the head, oppressed feeling in the chest, obese body and loose stool, and the accompanying symptoms as palpitation, anorexia, insomnia, tinnitus, lumbago, dry mouth, pink or dark purple and enlarged tongue with tooth prints, greasy tongue coating and taut slippery or soft thready pulse. Patients with any two main symptoms or accompanying symptoms plus the tongue and pulse conditions conform to the standard.

### Inclusion

Included are patients who conform to the above-mentioned diagnostic standard and without taking drugs for lowering blood pressure or stopped taking drugs for lowering blood pressure for 2 weeks.

### Exclusion

Excluded are patients with coronary heart disease, diabetes, cerebrovascular disease, incomplete renal function, smoking history, allergic constitution or allergy to many drugs, patients who have taken part in other clinical experiment in recent 3 months, patients with bad obedience judged by researchers, and patients who can not strictly implement the experimental plan.

## METHODS

### Method of Treatment

Single blind method (testees were in blind state) was used for clinical observation. In the treatment group, patients took *Yinian Jiangya Yin* (mainly consisting of Gou Teng (钩藤 *Ramulus Uncariae cum Uncis*) 20g (to be decocted later), Shi Jue Ming (石决明 *Concha Haliotidis*) 25g (to be decocted earlier), Cu Gui Jia (醋龟甲 *Plastrum Testudinis*) 20g (to be decocted

earlier), Fa Ban Xia (法半夏 *Rhizoma Pinelliae Praeparata*) 10g, Chen Pi (陈皮 *Pericarpium Citri Reticulatae*) 8g, Chao Zhi Ke (炒枳壳 *Fructus Aurantii*) 12g, Huai Niu Xi (怀牛膝 *Radix Achyranthis Bidentatae*) 25g, Yi Mu Cao (益母草 *Herba Leonuri*) 15g, Sang Ji Sheng (桑寄生 *Ramulus Loranthis*) 20g, and Zhi Shou Wu (制首乌 *Radix Polygoni Multiflori*) 20g). One dose was decocted with water into 200 ml every day. The decoction 100 ml was orally taken in the morning and in the evening respectively for 2 courses of treatment with 15 days as one course. Patients in the control group were treated with *Tianma Gouteng Yin* (consisting of Tian Ma (天麻 *Rhizoma Gastrodiae*) 9g, Gou Teng (钩藤 *Ramulus Uncariae cum Uncis*) 12g (to be decocted later), Shi Jue Ming (石决明 *Concha Haliotidis*) 18g (to be decocted earlier), Zhi Zi (栀子 *Fructus Gardeniae*) 9g, Huang Qin (黄芩 *Radix Scutellariae*) 9g, Chuan Niu Xi (川牛膝 *Radix Cyathulae*) 12g, Du Zhong (杜仲 *Cortex Eucommiae*) 9g, Yi Mu Cao (益母草 *Herba Leonuri*) 9g, Sang Ji Sheng (桑寄生 *Ramulus Loranthis*) 9g, Ye Jiao Teng (夜交藤 *Caulis Polygoni Multiflori*) 9g, and Fu Shen (茯神 *Poria cum Ligno Hospite*) 9g).<sup>4</sup> One dose was decocted with water into 200 ml every day. The decoction was orally taken with the same dosage, time and treatment course as in the treatment group.

### Indexes and Methods of Observation

Clinical syndromes: Dizziness, headache, heavy sensation in the head, oppressed feeling in the chest, obese body, loose stool, palpitation, anorexia, insomnia, tinnitus, lumbago, and dry mouth are classified for scoring before and after treatment.<sup>3</sup> No symptom is defined as score 0, mild symptom as score 1, moderate symptom as score 2 and severe symptom as score 3.

Blood pressure: Blood pressure of right upper arm is determined with an automatic electronic sphygmomanometer when patients take a sitting position. The determination begins after patients calmly take a rest for 15 minutes. Stage I and stage IV of Korotkoff sounds is taken as SBP and DBP respectively. The determination is carried out once every 3 minutes for 3 times and the average value of 3 determinations is

taken into the record. The readings of SBP and DBP before and after treatment are recorded.

ET and NO: After treatment, venous blood 2 ml taken from a patient and evenly mixed with the anti-coagulant 10% EDTA2Na 30  $\mu$ l and trasytol 40  $\mu$ l in a tube is centrifugalized in a refrigerated centrifuge at 4°C and 3000 r/min for 10 minutes. Separated plasma is stored in a refrigerator at -20°C. ET is determined with a SN-695B radio-immunity  $\gamma$ -measuring instrument produced by Shanghai Rihuan Instrument Factory and a reagent kit produced by Beijing Pulweiy Biological Sci-tech Co. Ltd. Venous blood 2 ml taken from a patient after treatment is put in a tube without the anti-coagulant for 20 minutes. Separated supernatant put in a centrifugal tube is centrifugalized at 3000 r/min for 10 minutes. Serum of upper layer is taken out and stored in a refrigerator at -20°C to be determined. Method of determination with nitrate reductase is used to determine NO with a UV-754 spectrometer and a reagent kit produced by Nanjing Jiancheng Bio-engineering Institute.

Safety: Under observation are possible adverse reactions in routine tests of blood, urine and stool as well as tests of hepatic and renal functions.

### Standard for Evaluation Therapeutic Effect

According to the standard in reference, obvious effect means that SBP decreases by 20 mmHg or more to normality or DBP decreases by 10 mmHg or more.<sup>3</sup> Effectiveness means that SBP decreases by less than 20 mmHg but to normality or DBP decrease by less than 10 mmHg but to normality. Ineffectiveness means that blood pressure remains at the same level as before treatment or even increases.

### Statistic Method

Statistical analysis is carried out with SPSS16.0

software package. ( $\bar{x} \pm s$ ) is used to express measurement data. Independent Sample Test is used for comparison between the two groups. Enumeration data are compared with  $\chi^2$  test.

## RESULT

### Comparison of Scores of TCM Syndrome Before and After Treatment in the Two Groups

As shown in Table 1, the score of TCM syndrome after treatment was less than that before treatment in the two groups ( $P < 0.05$ ). There was a statistical difference ( $P < 0.05$ ) in reduction in the score of TCM syndrome between the two groups, indicating that the improvement of syndrome in the treatment group is better than that in the control group.

Table 1. Comparison of scores of TCM syndrome before and after treatment in the two groups (score,  $\bar{x} \pm s$ )

Group	Cases	Before treatment	After treatment
Treatment group	40	9.38 $\pm$ 1.06	4.65 $\pm$ 1.00* <sup>△</sup>
Control group	39	9.05 $\pm$ 1.10	6.56 $\pm$ 1.10*

Note: \* $P < 0.05$  as compared to the datum before treatment in the same group; <sup>△</sup> $P < 0.05$  as compared to the datum after treatment in the control group.

### Comparison of Blood Pressure Before and After Treatment in the Two Groups

As shown in Table 2, there was no statistical difference ( $P > 0.05$ ) in SBP and DBP before treatment between the two groups, SBP and DBP after treatment were lower than those before treatment in the two groups ( $P < 0.01$ ), and there was a statistical difference ( $P < 0.01$ ) in SBP and DBP after treatment between the two groups, showing that the reduction in SBP and DBP in the treatment group is superior to that in the control group.

Table 2. Comparison of SBP and DBP before and after treatment in the two groups (mmHg,  $\bar{x} \pm s$ )

Group	Cases	SBP		DBP	
		Before treatment	After treatment	Before treatment	After treatment
Treatment group	40	155.65 $\pm$ 3.167	145.25 $\pm$ 3.319* <sup>△</sup>	94.18 $\pm$ 2.630	86.18 $\pm$ 2.630* <sup>△</sup>
Control group	39	155.23 $\pm$ 2.767	148.95 $\pm$ 2.695*	93.72 $\pm$ 2.305	88.79 $\pm$ 2.285*

Note: \* $P < 0.01$  as compared to the datum before treatment in the same group; <sup>△</sup> $P < 0.01$  as compared to the datum after treatment in the control group.

### Comparison of the Effect on Lowering Blood Pressure between the Two Groups

In the treatment group of 40 cases, the treatment was obviously effective on 8 cases, effective on 30 cases, and ineffective on 2 cases, with the total effective rate at 95.0%. In the control group of 39 cases, the treatment was effective on 34 cases and ineffective on 5 cases with the total effective rate at 87.2%. There was a statistical difference ( $P < 0.05$ ) in the total effective rate between the two groups, indicating that the effect in the treatment group is better than that in the control group.

### Comparison of ET and NO After Treatment between the Two Groups

There was no statistical difference ( $P > 0.05$ ) in the contents of ET and NO before treatment between the two groups. As shown in Table 3, there was a statistical difference ( $P < 0.05$ ) in the contents of ET and NO after treatment between the two groups. The ET content was lower and the NO content was higher in the treatment group than those in the control group.

Table 3. Comparison of ET and NO after treatment between the two groups ( $\bar{x} \pm s$ )

Group	Cases	ET (pg/ml)	NO ( $\mu\text{mol/L}$ )
Treatment group	40	39.09 $\pm$ 17.38*	59.04 $\pm$ 9.80*
Control group	39	47.01 $\pm$ 14.83	53.91 $\pm$ 10.83

Note: \* $P < 0.05$  as compared to the datum in the control group.

### Adverse Reaction

No abnormality was found in the examinations of hepatic and renal functions as well as in the routine tests of blood, urine and stool of the 79 patients after treatment.

### DISCUSSION

According to TCM theory, the authors hold that tendons not only link to muscles and joints but also attach to blood vessels to regulate vascular expansion and contraction. Because the liver governs tendons, vascular expansion and contraction are closely related to hepatic function. The main pathogenesis of primary hypertension is that hepatic

dysfunction can cause disordered circulation of *qi* and blood and abnormal expansion and contraction of blood vessels.<sup>5</sup> In the area of Guangzhou and Macao with sub-tropic climate, where people are found of cold tea and seafood and live a life with quick rhythm, early hypertension mainly belongs to the stagnation of phlegm and blood stasis in meridians and hyperactivity of the liver-*yang* in TCM syndromes. In the recipe of *Yinian Jiangya Yin* prescribed according to TCM pathological characteristics of early hypertension in the area, Gou Teng (钩藤 *Ramulus Uncariae cum Uncis*), Shi Jue Ming (石决明 *Concha Haliotidis*) and Cu Gui Jia (醋龟甲 *Plastrum Testudinis*) can calm the liver to suppress its *yang* hyperactivity; Fa Ban Xia (法半夏 *Rhizoma Pinelliae Praeparata*), Chen Pi (陈皮 *Pericarpium Citri Reticulatae*) and Chao Zhi Ke (炒枳壳 *Fructus Aurantii*) can dissolve damp, remove phlegm and promote *qi*-circulation to regulate the stomach; Yi Mu Cao (益母草 *Herba Leonuri*) can promote blood circulation and induce diuresis to clear meridians; Huai Niu Xi (怀牛膝 *Radix Achyranthis Bidentatae*), Sang Ji Sheng (桑寄生 *Ramulus Loranthi*) and Zhi Shou Wu (制首乌 *Radix Polygoni Multiflori*) can nourish the liver and kidney to treat the Ben-root. All ingredients of the recipe are used to jointly calm the liver, nourish tendons, remove phlegm and clear meridians. The result of the research showed that the effect of *Yinian Jiangya Yin* on improving TCM syndrome of patients with early hypertension and lowering blood pressure in the treatment group was better than that in the control group.

The medical circle has generally recognized the important role played by dysfunction of vascular endotheliocytes in causing hypertension and its pathological change. There is a negative feedback regulation between ET and NO, a pair of vascular systolic and diastolic factors, synthesized and released by vascular endotheliocytes in the physiological condition. The synthesis and release of ET and NO are in dynamic balance to jointly regulate vascular tension.<sup>6,7</sup> In hypertension, the balance is broken, making ET increase and NO decrease. The

result of the research showed that after treatment, decrease in ET and increase in NO were more obvious in the treatment group than those in the control group, indicating that with its effect on lowering the active ingredient for contracting blood vessels and increasing the active ingredient for expanding blood vessels, *Yinian Jiangya Yin* can regulate the imbalance between ET and NO of patients with early hypertension. To sum up, the effect of *Yinian Jiangya Yin* on improving syndrome and lowering blood pressure may be related to its regulating the imbalanced ET and NO for restoring the function of endothelium-dependent vasodilation.

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